Doxycycline-induced Dizziness in Dental Patient

CASE REPORT

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Abstract

Many dentists are unaware of the documented adverse drug reaction of doxycycline: induced dizziness. Because doxycycline is frequently prescribed in dentistry, it is important for dentists and patients to be aware of this significant adverse reaction to prevent medical complications. A clinical case is reported in which a patient developed dizziness after taking doxycycline that was prescribed following periodontal surgery. The dizziness resolved when the doxycycline was stopped. Patients and dentists should be educated to recognize the signs and symptoms of doxycycline's adverse reactions.

DIZZINESS is a subjective feeling that is often difficult to quantify. The causes of dizziness are multifactorial and include high blood pressure, multiple medications (e.g., antihypertensives and narcotics). Different medical conditions are associated with dizziness, including vertigo, low glycemic level and ear problems. Because dizziness can be a serious problem, we propose through this article to help dentists understand how patients could develop dizziness from taking doxycycline.

The etiology of doxycycline-induced dizziness is complex, subjective and relatively unclear. This adverse drug reaction may have a higher incidence than documented in the literature. Additionally, dentists prescribing tetracyclines, including doxycycline and minocycline, should be aware of a condition of increased intracranial pressure and pay particular attention to a patient who complains of developing a new headache, dizziness or visual impairment.

Doxycycline hyclate is indicated in the adjunctive treatment of aggressive periodontal infections in which *Aggregatibacter actinomycetemcomitans* (formerly known as *Actinobacillus actinomycetemcomitans*) is often the causative pathogen that invades the epithelium and connective tissue, eluding mechanical debridement.[1] Doxycycline and minocycline are semisynthetic analogs of tetracycline HCl. Doxycycline is available in two salt forms.

- Doxycycline monohydrate is used primarily in the treatment of acne.
- Doxycycline hyclate is used as an antibiotic and as an anticollagenase, nonantimicrobial agent for the treatment of chronic periodontitis in adults.[2]

Dentists should be aware of a particular adverse drug reaction, whereby doxycycline can induce dizziness when it is taken systemically in the adjunctive treatment of periodontal infections. We highlight the clinical presentation of a patient with doxycycline-induced dizziness and discuss the etiology, signs and symptoms.

Case Report

A 58-year-old Caucasian male presented for regenerative periodontal therapy in November 2008. The patient was not taking any over-the-counter drugs, prescription drugs or neutraceuticals. The surgical area encompassed teeth #13 through #15. Full thickness flaps were elevated after 2% lidocaine with 1:100,000 epinephrine was utilized for local anesthesia.

After scaling and root planing and osseous resection, bone grafts were placed into the remaining two wall osseous defects by #14 and #15. Four 4-0 silk sutures and Coe-Pak were placed. Hemostasis was achieved. Postoperatively, the patient was given a prescription for doxycycline hyclate 100mg capsules for 10 days: 200 mg loading dose (taken in the evening) followed by 100 mg every morning and ibuprofen 600 mg (one tablet every four to six hours when needed for pain).[3] The patient was given both verbal and written instructions on the proper use of doxycycline. This regimen for doxycycline is indicated for both dental and medical infections.[4-8]

The patient called the office four days later to report that he had arrived home the night of the surgery and took his doxycycline as directed. However, he didn't take any of the ibuprofen because he felt it wasn't necessary. At 4 a.m. the next day, he got up from his bed to use the bathroom. He felt dizzy and passed out. He bumped his head and was taken to the hospital with no memory of ever falling—there is only one other case report documenting amnesia, which occurred after a sudden onset of a headache following the ingestion of 200 mg of doxycycline.[9]

The computed tomography (CT) scan was negative and the patient was sent home. He was instructed by the physician to continue taking his medications. The following morning when he got up from bed, he felt dizzy again, but he got up carefully and slowly.

The patient returned to the office eight days after surgery for postoperative suture and pack removal. Healing was uneventful. The patient's blood pressure was taken and was 128/78 with a pulse of 71. He reported getting dizzy spells when he awoke, but the dizziness quickly passed when he rose. It was recommended that the patient stop taking the antibiotic, and he was referred to his physician for evaluation. The patient reported in a subsequent interview and again when he returned for his three-month periodontal maintenance appointment that the dizziness disappeared after he stopped taking the doxycycline.

Discussion

Antibiotic-induced adverse drug reactions play a pivotal role in the overall health care of the patient, including increased office and hospital costs for treatment.[10] Reducing the incidence of adverse reactions starts with clinician and patient education.

Table 1 lists adverse reactions to doxycycline according to body systems. Sometimes the patient may experience an adverse reaction and neither the patient nor the dentist attributes it to the drug itself but rather to a medical condition. For example, doxycycline prescribed by the dentist has been documented to cause esophageal

TABLE 1

Adverse Reactions of Doxycycline[32, 33]

CNS: dizziness, headache, intracranial hypertension, visual changes.

CV: pericarditis.

DERM: photosensitivity reactions (exaggerated sunburn), skin rash, pigmentation changes.

ENDOCRINE: brown/black discoloration of thyroid gland (no dysfunction), hypoglycemia.

GI: nausea, vomiting, diarrhea, abdominal pain, esophageal ulcers, dyspepsia, psuedomembranous colitis (due to Clostridium difficle), anorexia.

HEMATOLOGIC: hemolytic anemia, neutrophenia, thrombocytopenia, eosinophilia.

HEPATIC: hepatotoxicity.

HYPERSENSITIVITY REACTIONS: urticaria, anaphylaxis.

ORAL: tooth discoloration, black hairy tongue (candidiasis), taste alterations, increased thirst, sore throat, odynophagia (painful swallowing), esophagitis.

RENAL: rise in BUN (blood urea nitrogen) levels.

TABLE 2

Patient Instructions[3]

- Stop taking medication if dizziness, sudden onset of new headache or disturbance in vision occurs. Notify dentist and physician immediately.
- Slowly get up from sitting position to avoid dizziness.
- Doxycycline should be taken on empty stomach, one hour before and two hours after eating; however, if there is GI upset, take it with food.
- Do not take concurrently with any antacid product that contains aluminum, bismuth salts, calcium and magnesium or any other product containing zinc or iron. Wait two hours before or after when consuming these products.
- It is recommended to avoid intake of dairy products, due to a 20%-30% decrease in doxycycline absorption.
- Doxycycline should be taken with full glass of water and in upright position to reduce risk of esophageal ulcers and irritation.
- Do not lie down for at least two hours after taking dose of doxycycline.
- If experiencing swallowing difficulties or chest pain, patient should notify dentist or physician immediately.
- Avoid exposure to direct sunlight and ultraviolet light during and for four to five days after discontinuing therapy. Sunscreens provide little protection against phototoxicity.
- Use of doxycycline may make oral contraceptives less effective; advise using alternative birth control methods.
- Use of doxycycline might increase incidence of vaginal candidiasis.
- Notify physician and dentist immediately if diarrhea occurs.

ulcers. The symptoms of a sore throat and odynophagia (difficulty in swallowing) experienced by the patient may not be thought to be caused by the drug itself. The patient, however, believes he or she is experiencing a possible cold and usually reports the symptoms directly to the physician rather than to the treating dentist.[3]

One central nervous system adverse reaction that has been reported occasionally in the medical literature but not in the dental literature is doxycycline-induced dizziness.[11-13] Thus, it should be noted that the dosing of doxycycline in some medical studies may not be the same as what is required for dental infections. The usual dosage of oral doxycycline is 100 mg every 12 hours on the first day, then 100 mg a day as a single dose (maximum is 100 mg every 12 hours) for up to 21 days.[5-8]

A clinical medical study compared adverse reactions following administration of either minocycline (100 mg at bedtime for 7 days) or doxycycline (100 mg twice daily for 7 days) to patients. It must be noted that only medical references are included in this article, because there are no documented dental studies. Results indicated that the most significant adverse effect was gastrointestinal upset, dizziness, nausea, vomiting, abdominal pain or cramps, diarrhea, dyspepsia, increased flatulence and taste alteration.[13] Vomiting alone ($P = 0.004$) or any gastrointestinal upset, including vomiting ($P < 0.001$), occurred significantly more often in the doxycycline group.

The occurrence of dizziness ($P > 0.1$) or other adverse effects did not differ between the two groups. However, when adverse effects were examined by drug regimen and gender, significance was again shown. Men and women who were administered doxycycline reported side effects more frequently than those in the minocycline group. Dizziness was reported in 9% of the patients: 5% of men and 13% of women.[13]

Patient instructions on taking doxycycline should be both verbal and written. Table 2 lists important points that must be discussed with the patient, including how and when to take the medication and what signs and symptoms could be expected.

The dizziness experienced in our patient may be related to a medical condition referred to as pseudotumor cerebri (PTC), also known as intracranial hypertension, which is a self-limiting condition that causes elevated intracranial pressure.[14,15] It has been reported to be caused by medications used to treat skin disorders, including tetracyclines (minocycline, doxycycline), retinoids and corticosteroids.[16-18] This condition commonly causes throbbing headache, blurred vision, vision loss, nausea, vomiting and dizziness. In most cases, the symptoms improve when doxycycline is stopped.

Although all tetracyclines (tetracycline HCl, doxycycline and minocycline) are implicated in PTC, doxycycline is the least reported probably because the "older" documented literature is on patients with acne, in which doxycycline is usually not prescribed.[17] Additionally, there is a 27.3% incidence of headache after locally applied doxycycline (Atridox) and a 9% incidence after minocycline and scaling (Arestin).[19,20] There are no published studies that show these headaches have any association with PTC.

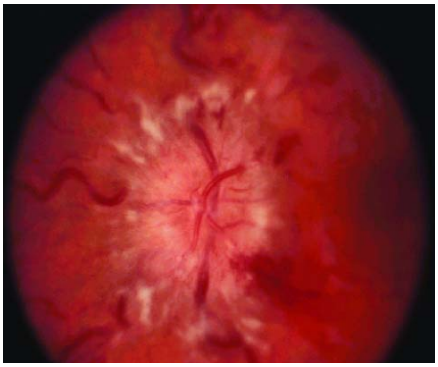

Figure1. Pseudotumor cerebri finding of disc swelling or edema upon ophthalmologist viewing back of eye.[34] Optic disc is where ganglion cell axons leave eye to form optic nerve. Swelling of disc occurs when there is increased intracranial pressure.

The cause of doxycycline-induced PTC is relatively unknown; however, one proposed mechanism by which doxycycline causes intracranial hypertension may include interference with the energy-dependent absorption mechanism by affecting cyclic adenosine monophosphate (cAMP, a messenger important in many biological processes that is synthesized from ATP) at the arachnoid granulations,[18,20] which are small projections of the arachnoid (membrane covering the brain) into the venous sinuses of the brain, which permit cerebrospinal spinal fluid to exit the brain.

Idiopathic, non-medication-induced pseudotumor cerebri most frequently occur in obese women in their 30s and 40s. However, tetracycline usage should be considered as the etiologic agent in patients with signs and symptoms of PTC who are not obese and can be male or female and any age group.[16,17]

Diagnosis of intracranial hypertension is based on physical examination, neuroimaging and lumbar puncture. The only neurologic sign is raised intracranial pressure. Otherwise, the computed tomography (CT scan) and magnetic resonance imaging (MRI) are normal, which is a finding in patients with PTC.[17,18] This may lead to permanent damage of the optic nerve and associated decrease in vision. There are ophthalmologic changes with the development of papilloedema, which is swelling of the optic disc caused by increased intracranial pressure[18,21] (Figure 1).

It is not well known how soon after starting the drug doxycycline-induced PTC develops, but it can show up within two weeks[18,22] and may be related to dosage.[23] However, because the exact etiology of doxycycline-induced PTC is relatively unclear, it cannot be ruled out even at lower dosages; therefore, the patient should still be monitored for it.[23] Thus, even at subantimicrobial doses of 20 mg, there could be an increased incidence of this adverse effect, although it has never been documented. Additionally, since the locally applied minocycyline and doxycycline products may be absorbed systemically, dizziness is also plausible. The dentist should not dismiss a patient's complaint of a newly developed headache, dizziness or visual disturbance, such as blurred vision. If PTC is suspected, the patient should be referred to a neurologist and ophthalmologist. Treatment involves terminating the tetracycline with resolution of the intracranial hypertension over two to four weeks.[24] Early diagnosis by the dentist is important. The outcome of treatment is good if PTC is recognized early to prevent permanent visual loss.[17]

The patient should be questioned as to when the symptoms appeared in relation to taking the tetracycline. It must be determined if the dizziness is originating from the disease or infection that patient has or from the doxycycline that is being used to treat the condition. For example, one of the symptoms of Lyme disease from a tick bite is dizziness and doxycycline is also used to treat the disease.[12] Dentists prescribing tetracyclines, including doxycycline and minocycline, should be aware of the condition of increased intracranial hypertension (pseudotumor cerebri) and pay particular attention to a patient who complains of a new headache, dizziness or blurred vision. Increased intracranial pressure can lead to progressive visual impairment and blindness in 4% to 12% of patients.[21]Thus, once the diagnosis of PTC is suspected, immediate therapy should be started to prevent visual damage.[21]

Additionally, doxycycline should be prescribed with caution to women of childbearing age who are overweight or have a history of idiopathic intracranial hypertension.[22]

Furthermore, dizziness or lightheadedness can be a symptom of orthostatic hypotension. In our case, physicians ruled out orthostatic hypotension (also referred to as postural hypotension), which occurs when there is a rapid lowering in blood pressure upon assuming an upright position. It is characterized by a decrease in systolic blood pressure of 20/10 mmHG and a decrease in diastolic blood pressure of 10 mmHG within three minutes of standing.[25]

Generally, the use of systemic antibiotics should not be considered as the sole therapy in clinical dentistry and should be used adjunctively. The authors agree with many clinical studies[26-29] that showed that improved clinical outcomes often do not result from the use of antibiotics. Thus, antibiotics may not be necessary for routine periodontal and oral surgical procedures. However, antibiotics can be considered as part of pre- or postsurgical therapy when periodontal osseous or soft-tissue grafts are placed because these newly placed grafts have not yet established a blood supply (revascularization) with the host bone or tissue.[30] Until a blood supply is established with inflammatory cells that may reduce the incidence for infection, an antibiotic regimen may be enforced.

The dizziness experienced by the patient in this report may have been due to the stress of the surgery. Stress has been shown to cause and exacerbate dizziness.[31] However, there is very little literature on the subject and none that we could find pertaining to periodontal surgery.

Conclusion

The dentist and patient must be aware that dizziness may be a relatively common but, possibly, not properly reported complication of doxycycline. Besides discontinuing the offending tetracycline, another tetracycline should not be prescribed, including subantimicrobial doses of 20 mg doxycycline. If PTC is suspected, the patient should be taken off the doxycycline and referral to a neurologist or ophthalmologist may be necessary. ■

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